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Respiratory Medicine (2008) **102**, 593–604

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Received 23 March 2007; accepted 6 November 2007
Available online 20 December 2007

KEYWORDS
Dry powder inhaler;
Inhalation technique;
Asthma;
COPD

Summary
Background: Incorrect usage of inhaler devices might have a major influence on the clinical effectiveness of the delivered drug. This issue is poorly addressed in management guidelines.
Methods: This article presents the results of a systematic literature review of studies evaluating incorrect use of established dry powder inhalers (DPIs) by patients with asthma or chronic obstructive pulmonary disease (COPD).
Results: Overall, we found that between 4% and 94% of patients, depending on the type of inhaler and method of assessment, do not use their inhalers correctly. The most common errors made included failure to exhale before actuation, failure to breath-hold after

Abbreviations: COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; FEV_1, forced expiratory volume in 1 s; pMDI, pressurised metered dose inhaler..

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0954-6111/$ - see front matter
doi:10.1016/j.rmed.2007.11.003

inhalation, incorrect positioning of the inhaler, incorrect rotation sequence, and failure to execute a forceful and deep inhalation. Inefficient DPI technique may lead to insufficient drug delivery and hence to insufficient lung deposition. As many as 25% of patients have never received verbal inhaler technique instruction, and for those that do, the quality and duration of instruction is not adequate and not reinforced by follow-up checks.
Conclusions: This review demonstrates that incorrect DPI technique with established DPIs is common among patients with asthma and COPD, and suggests that poor inhalation technique has detrimental consequences for clinical efficacy. Regular assessment and reinforcement of correct inhalation technique are considered by health professionals and caregivers to be an essential component of successful asthma management. Improvement of asthma and COPD management could be achieved by new DPIs that are easy to use correctly and are forgiving of poor inhalation technique, thus ensuring more successful drug delivery.

Introduction

Drugs for inhalation are the cornerstone of therapy in obstructive lung disease.[1,2] Inhalers are the principle vehicles for the effective administration of asthma medication. They allow high lung deposition of the drug and minimise systemic bioavailability, thus reducing possible systemic adverse drug reactions.[1,2] Pressurised metered dose inhalers (pMDIs) and dry powder inhalers (DPIs) are the devices most commonly used for drug delivery in the treatment of asthma and chronic obstructive pulmonary disease (COPD). DPIs, available since the 1970s, have been developed to make inhalation simpler compared with pMDIs, without the need to coordinate inhalation and actuation.[3,4] DPIs are easier to use than pMDIs because they are breath-activated, precluding the need for the patient to coordinate actuation with inhalation, which can be particularly difficult for some patients, including the elderly and children. This assists with effective drug delivery to the lungs. In addition, DPIs do not contain environmentally unfriendly propellants and do not produce a cold sensation on inhalation. DPIs are single or multiple dose inhalers that require loading before inhalation as they are breath-actuated.[1,3]

The effectiveness of drugs for inhalation such as β_2-agonists, anticholinergic agents or corticosteroids, can be influenced by many factors including age, sex and education of the patient, duration of disease, type of inhaler used, correct inhalation technique or use of several inhalers.[5–9] Many elderly people have poor inhalation technique because of medical problems such as arthritis, weakness or impaired dexterity or vision.[10] Correct inhalation technique plays a vital role in effective asthma therapy alongside appropriate drug usage.[11] Incorrect usage of inhalers is a significant problem for both asthma and COPD management because it may result in diminished therapeutic effect, resulting in poor control of symptoms and thereby insufficient disease management.[5–7,12,13] As a result, patients might receive treatment, but without proper education and training in correct inhalation technique, the therapeutic benefit is less than optimal.

Technical features of inhaler devices have improved constantly with time. However, the effectiveness in delivering drugs to the lungs depends on correctly performed inhalation manoeuvres. In previous studies, it has been shown that up to 85% of patients do not use their inhalers correctly.[9,14,15] Many inhalers, both pMDIs and DPIs, are complicated to use, some requiring up to eight steps for a correctly performed inhalation manoeuvre.[16] To acquire the skills required for using these medications, health professionals and patients must be adequately educated and trained.[17,18] Asthma management might improve with devices which are easy to use correctly and have feedback mechanisms confirming correct inhalation and assured drug delivery.[11]

The objective of this review was to assess the incidence of incorrect inhaler technique with established DPIs in patients with asthma or COPD, to highlight the most common errors observed in inhalation technique and to discuss implications for clinical efficacy.

Materials and methods

Search strategy

The search strategy included primary and secondary sources. MEDLINE (1966–2005) and EMBASE (1988–2005) were used for the search in primary sources with the following keywords: 'mishandlings', 'errors' or 'incorrect use' in conjunction with the keyword 'dry powder inhaler'. The titles and abstracts of all articles produced by this search were assessed for inclusion prior to retrieval of full articles. All full articles were then subsequently reassessed for inclusion, and only those dealing with inhaler technique and meeting the inclusion criteria were included in the analysis. There was no blinding of authors' names or institutions and no scoring system was used. We also performed a manual search of the 15 most popular journals (published between 2000 and 2005 by impact factor) on respiratory diseases. This manual search included an assessment of the title and abstract of all articles in these journals. A search of secondary sources involved scanning all references from the publications identified in the search of the primary sources. Both searches were limited to human studies.

Inclusion/exclusion criteria

Adult and paediatric studies were included in the analysis. Only asthma and COPD studies addressing DPI usage were

assessed for inclusion. Publications in English, Spanish, French, Italian, German or Portuguese were included in the analysis.

Commentaries, cost-analyses, surveys, letters to editors and guidelines were excluded.

Results

The search of primary sources identified 47 articles on incorrect use of DPIs in the management of asthma or COPD. Secondary sources provided three more articles.

Misuse of DPIs

Studies in adult patients

DPIs are widely used in clinical practice; however, a number of studies have shown that many patients do not use currently established inhalers correctly, with the type of inhaler contributing significantly to the rate of incorrect usage (Table 1).[5,9,10,12,14,16,19–39] Indeed between 4% and 94% of patients, depending on the type of inhaler and method of assessment, do not use their DPIs correctly (Table 1). Molimard et al.[12] conducted an observational study of 3811 patients with asthma or COPD. Patients were treated for at least 1 month with drugs delivered through pMDIs or DPIs, namely the Aerolizer® (Novartis, USA), Diskus® (GlaxoSmithKline, UK) or Turbuhaler® (AstraZeneca, UK).[12] Results showed that 76% of the patients using pMDIs made at least one error compared to 49–55% of the patients using DPIs, indicating differences in the use of inhaler devices in 'real life' clinical practice and also highlighting the fact *that* pMDIs are more difficult to use than DPIs.[12] Similarly, Hilton[19] conducted a study to evaluate the DPI inhalation technique of 422 patients from 34 clinical practices. In that study, technique scores were rated as 'good', 'adequate' or 'inadequate'. Overall, 25% of the patients had an inadequate technique.[19] More specifically, 4% of patients were unable to use the Turbuhaler® correctly compared with 21% and 19% for the Rotahaler® (GlaxoSmithKline, UK) and Diskhaler® (GlaxoSmithKline, UK), respectively.[19] It is not surprising that such a high proportion of patients were unable to use the Diskhaler® correctly as it is too complicated to use, requiring eight steps to affect a correct inhalation. Additionally, with the Diskhaler® the drug blisters must be frequently changed, the device must be cleaned before refilling and it provides the patient with no feedback except for a sweet taste in the mouth which may simply be indicative of high oropharyngeal deposition. Patients frequently fail to pierce the drug blisters top and bottom and may cover the air inlet holes with their mouths whilst inhaling due to incorrect mouthpiece positioning. In another study van der Palen et al.[14] assessed inhaler technique of the Turbuhaler®, Rotahaler® and Diskhaler®. Errors were recorded against a predefined list of steps for each inhaler. The results showed that 40% of the patients were unable to perform all steps correctly. Other studies have shown even higher rates of misuse for the Turbuhaler® ranging from 26% to 94% (Table 1).[5,9,12,21,22,25,26,29,30,33–35,39] Common mistakes when using the Turbuhaler® include failure to turn the base fully in both directions and failure to keep the device upright until loaded. In addition, the Turbuhaler® has a relatively high intrinsic resistance making it difficult to generate a sufficient inspiratory flow in order to desagglomerate and release drug particles. This may be particularly relevant for elderly patients, children and those patients with severe airflow limitation.

Kesten et al.[23] evaluated use of the Diskhaler® in a 2-week study with 4529 patients with reversible obstructive airway disease who required β_2-agonist treatment. Although the majority of the patients (98.5%) used the Diskhaler® correctly after instructions at the beginning of the study, incorrect use was noted at the end of the trial mandating the need and importance for regular instruction.[23] The overall results from the study showed that 10.2% of the elderly patients and 3.2% of the patients in all other age groups combined did not use the Diskhaler® correctly.[23] In the present review, we found that as many as 68% of patients misuse their Diskhaler® and as many as 67% misuse their Rotahaler®.[16,21] Other DPIs fare slightly better with up to 57% of patients unable to use their Diskus® correctly.[12,29,34,36,39] The mouthpiece of the Diskus® has frequently been cited as user-unfriendly; in addition, due to its drug blister design, incomplete emptying of the metered dose may occur.[40] We found evidence that 11% of patients were unable to use the Cyclohaler® (Pharmachemie, the Netherlands) correctly,[5] 12–17% incorrectly used the Aerolizer®[12,32,34] and up to 55% misused the Easyhaler® (Table 1).[37,39] The Easyhaler® should be shaked before use and the active ingredient may escape if patients exhale into the system.[40] Since the Aerolizer®, like the Diskus®, may suffer from incomplete emptying of the metered dose, the inhalation manoeuvre could be repeated with an increased risk of overdosing.

Studies in children and adolescents with asthma

In children, as well as in adults, correct use of inhalers is vital for the management of asthma and other respiratory diseases. Most children do not, however, use their inhalers correctly and the ability to correctly use an inhaler positively correlates with age. Studies have shown that children experience the same problems as adults in the correct use of inhalers.[6,7,41–43] Table 2 shows percentages of children who did not perform the inhalation technique correctly in a number of studies using different DPIs. Pedersen et al.[6] conducted a study for 4 months to assess the correct use of inhalers in 256 children aged 4–16 years. They showed that 54% of these children were unable to use the Rotahaler® correctly.[6]

Children fared no better with the Turbuhaler®. The clinical efficacy of terbutaline sulphate delivered through the Turbuhaler® was evaluated in 59 children aged between 3 and 6 years by scoring the clinical state of asthma before and 10 min after drug inhalation.[7] Inhalation technique was evaluated by using a graded score and the clinical response using three variables: inspiratory wheezing, expiratory wheezing and prolonged expiration.[7] The results showed that 57% of the 4-year-old children, 33% of the 5-year-old children and 20% of the 6-year-old children did not use the inhaler correctly; indeed, all 3-year-old children were unable to perform the inhalation technique correctly.[7] De Boeck et al.[41] confirmed this age-dependent relationship

Table 1 Characteristics of studies involving adult patients with asthma and COPD included in the review.

Study	No. of patients	Type of inhaler	% of patients with incorrect inhalation technique
Hesselink et al.[5]	558	Diskhaler®	4
		Cyclohaler®	11
		Rotahaler®	37
		Turbuhaler®	31
van der Palen et al.[9]	321	Turbuhaler®, Diskhaler®, Cyclohaler®, Ingelheim inhaler®, Rotahaler®	29
Franks et al.[10]	80	Multidose DPI	25 errors*
		Capsule DPI	6 errors*
Molimard et al.[12]	3811	Aerolizer®	54
		Diskus®/Accuhaler®	49
		Turbuhaler®	54
van der Palen et al.[14]	152	Turbuhaler®, Diskhaler®, Rotahaler®	40
van Beerendonk et al.[16]	316	Diskhaler®	49
		Rotahaler®	67
		Ingelheim inhaler®	36
Hilton[19]	422	Turbuhaler®	4
		Rotahaler®	21
		Diskhaler®	19
Dompeling et al.[20]	50	Rotahaler®	27
Nimmo et al.[21]	20	Diskhaler®	68†
		Turbuhaler®	94†
van der Palen et al.[22]	123	Diskhaler®	14
		Rotahaler®	65
		Turbuhaler®	54
Kesten et al.[23]	4529	Diskhaler®	10 in the elderly patients 3 of all other age groups combined
Olaguibel Rivera et al.[24]	296	DPIs	30
van der Palen et al.[25]	50	Diskus®/Accuhaler®	8
		Turbuhaler®	26
Campos et al.[26]	150	Turbuhaler®	42
Cimas et al.[27]	34	Turbuhaler®	26
Carrion-Valero et al.[28]	554	Turbuhaler®	59
Serra-Battles et al.[29]	169	Diskus®	30
		Turbuhaler®	31
Estarriol et al.[30]	186	Turbuhaler®	68
Aiolfi et al.[31]	71	Pulvinal®	18
Cinti et al.[32]	158	Aerolizer®	17
Canessa et al.[33]	309	Turbuhaler®	48
Girodet et al.[34]	984	Turbuhaler®	38
		Aerolizer®	12
		Diskus®	13
Botting et al.[35]	188	Turbuhaler®, Diskhaler®	33
Kamin et al.[36]	1423	Turbuhaler®	39
		Diskus®	17
Giner et al.[37]	30	Diskus®/Accuhaler®	0
		Easyhaler®	0
		Turbuhaler®	0

Table 1 (*continued*)

Study	No. of patients	Type of inhaler	% of patients with incorrect inhalation technique
Ho et al.[38]	500	Various breath-activated devices	28
Rönmark et al.[39]	326	Easyhaler®	55
		Diskus®/Accuhaler®	57
		Turbuhaler®	49

*Number of errors made by patients; DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler.
†Following written instruction alone.

Table 2 Characteristics of studies involving paediatric asthma patients included in the review.

Study	No. of patients	Type of inhaler	% of children with incorrect inhalation technique
Pedersen et al.[6]	256	Rotahaler®	54
Goren et al.[7]	59	Turbuhaler®	3-year old: 100 4-year old: 57 5-year old: 33 6-year old: 20
De Boeck et al.[41]	161	Turbuhaler®	>8 years: 4 5–8 years: 45
Gracia-Antequera and Morales Suarez-Varela[42]	255	DPI	39
Kamps et al.[43]	200	Turbuhaler®, Diskhaler®, Diskus®/ Accuhaler®	22

DPI, dry powder inhaler.

showing that only 4% of children over 8 years were unable to use the Turbuhaler® compared with 45% of children aged between 5 and 8 years.

A study by Kamps et al.[43] showed that up to 80% of children did not use the inhaler correctly when the instructor demonstrated the technique, but that education and training improved inhalation technique in these children and adolescents.[43] Overall, analysis showed that repetition of the instructions was significantly correlated with correct inhalation technique ($p<0.0001$) irrespective of the type of inhaler used.[43] In a similar study Gracia-Antequera and Morales Suarez-Varela[42] assessed the inhalation technique of 255 children and adolescents using DPIs and pMDIs before and after training. The results showed an increased (76%) frequency of correct use after training compared with baseline (47%).[42] However, it is worth noting that a significant number of patients (24.5%) were still not able to use their devices correctly even after instruction.[42]

Specific errors in DPI technique

The main determinants of incorrect inhaler use are compliance, type of inhaler, use of several inhalers, patients' characteristics and low emotional quality of life.[5,9] It has been shown that patients using pMDIs make more errors than users of other types of inhalers.[5] Children newly referred to asthma clinics were found to make more errors with inhalers, possibly because of lack of re-assessment and re-enforcement of their technique.[43]

Incorrect use of inhalers can lead to detrimental effects on asthma management[44]; nevertheless, studies have shown that patients do not comply with the individual steps of the inhalation maneouvre.[2] Table 3 summarises studies involving adult and paediatric patients with asthma exhibiting specific errors in inhalation technique with established DPIs. The most frequently observed error was failure to exhale before inhaling through their DPI device (12–77%). A comfortable exhalation to, or just below functional residual capacity is an accepted alternative to exhalation to residual volume, being less likely to provoke cough while still retaining efficacy.[45] Other specific inhalation technique errors in order of frequency included failure to breath hold after inhalation (0–73%); failure to forcefully and deeply inhale through the device (0–48%); incorrect dose metering (1–46%); incorrect rotation sequence (i.e. rotation of grip until 'click' is heard, 0–45%); incorrect inhaler position (0–44%); failure to breathe out slowly after inhalation

Table 3 Characteristics of studies performed in patients with asthma and COPD exhibiting specific errors in dry powder inhaler technique.

Study	Type of inhaler	Type of error							
		Incorrect dose metering	Incorrect inhaler positioning	Incorrect rotation sequence	No exhalation before activation	Incorrect mouthpiece positioning	No forceful and deep inhalation	No breath hold	Failure to breathe out slowly
Hesselink et al.[5] ($n = 558$)	Diskhaler®	3	–	–	–	–	2	–	–
	Cyclohaler®	1	9	–	–	–	0	–	–
	Rotahaler®	–	34	3	–	–	1	–	–
	Turbuhaler®	–	29	2	–	–	2	–	–
Pedersen et al.[6] ($n = 256$)	Rotahaler®	46	–	–	62	–	41	49	–
van der Palen et al.[9] ($n = 321$)	Accuhaler®	–	0	–	25	0	–	0	–
	Cyclohaler®	0	0	–	40	0	0	30	–
	Diskhaler®	2	–	10	28	7	9	16	–
	Ingelheim inhaler®	0	–	–	12	0	0	0	–
	Rotahaler®	2	32	2	53	4	7	34	–
	Turbuhaler®	–	29	2	38	2	2	17	–
Molimard et al.[12] ($n = 3811$)	Aerolizer®	1	–	–	33	–	–	29	–
	Diskus®	–	–	–	30	–	–	26	–
	Turbuhaler®	–	18	15	30	–	–	25	–
van der Palen et al.[14] ($n = 152$)	Diskhaler®	4	–	–	44	4	0	37	19
	Rotahaler®	4	37	0	66	21	10	54	21
	Turbuhaler®	–	31	0	66	28	6	41	16
van Beerendonk et al.[16] ($n = 316$)	Different types of DPI	14	7	–	66	4	19	53	–
Dompeling et al.[20] ($n = 50$)	Rotahaler®	–	32	0	68	–	2	44	–
	Diskhaler®	32	0	–	58	26	26	32	32

Nimmo et al.[21] ($n = 20$)*	Turbuhaler®	38	44	44	44	19	25	31	31
van der Palen et al.[22] ($n = 123$)	Diskhaler®	–	0	–	64	29	14	50	43
	Rotahaler®	14	31	45	71	20	22	73	35
	Turbuhaler®	15	31	38	77	35	19	61	15
Kesten et al.[23] ($n = 4529$)	Diskhaler®	1.0	–	–	–	–	1.0	–	–
Olaguibel Rivera et al.[24] ($n = 296$)	DPIs	14	–	–	–	–	10	32	–
van der Palen et al.[25] ($n = 50$)	Diskus®	8		–	40	0	0	6	2
	Turbuhaler®	14	12	–	38	0	0	6	2
Campos et al.[26] ($n = 150$)	Turbuhaler®	–	10	10	–	5	10	–	–
Estarriol et al.[30] ($n = 186$)	Turbuhaler®	23	18	–	58	13	48	68	–
Cinti et al.[32] ($n = 158$)	Aerolizer®	–	–	–	–	6	11	–	–
Canessa et al.[33] ($n = 309$)	Turbuhaler®	15	–	–	13	–	15	–	–
Ghirodet et al.[34] ($n = 984$)	Aerolizer®	5	–	–	40	–	–	33	–
	Autohaler®	–	–	–	28	–	–	37	–
	Diskus®	–	–	–	40	9	–	36	–
	Turbuhaler®	–	22	13	37	–	–	32	–
De Angelis et al.[52] ($n = 358$)	Diskus®	–	–	–	18	–	–		–

For each considered study, values represent the percentage of patients showing specific errors in the use of dry powder inhaler (DPI).
*After written instruction only.

(2–43%); and incorrect mouthpiece position (i.e. not positioning the mouthpiece correctly between the lips, 0–35%).

The three most frequent errors made by patients for each DPI are reported in Table 4. Irrespective of the device employed, the most frequent error was failure to exhale before inhaling through their DPI (Table 4). This is important, as without an adequate exhalation patients may be unable to inhale forcefully and deeply enough through their DPI in order to ensure deposition of drug into the lungs. The second most frequent error for most devices was failure of patients to hold their breath after they had completed inhaling through the device. The exceptions to this finding were with the Diskhaler® and the Turbuhaler® where the second most frequent error exhibited by patients was due to incorrectly performed metering of the dose and incorrect inhaler positioning, respectively. The third most frequent error varied according to device. For the Rotahaler® and Cyclohaler®, it was incorrect inhaler position, for both the Diskhaler® and Turbuhaler® it was failure by patients to breath hold; for the Diskus® and Aerolizer® it was incorrect dose metering; and for the Autohaler® it was incorrect mouthpiece positioning (Table 4).

Whilst all inhaler errors have the potential to limit clinical efficacy, some errors are more important than others in this respect. Molimard et al.[12] defined lack of exhalation before inhalation and failure to breath-hold post-inhalation as device-independent errors.[12] Inhaler errors were defined as critical if they could have substantially affected dose delivery to the lung. Critical errors for all DPIs included lack of inhalation through the mouthpiece and blowing into the device before inhalation.[12] However, it should be noted that exhaling into a DPI would be of greater significance with bulk reservoir devices such as the Turbuhaler®, but less so for the Diskus® in which unit doses are sealed until priming. Device-specific critical errors were lack of capsule insertion and lack of two-button press and release for the Aerolizer®, not raising the lever to the vertical position whilst using the Autohaler® and not sliding the lever as far as possible whilst using the Diskus®.[12] Critical errors likely to affect clinical efficacy whilst using the Turbuhaler® included not holding the inhaler in the upright position for grip rotation and also incorrect rotation sequence.[12] Generally, the most important error in the use of a DPI is failure to achieve a forceful and rapid inspiratory flow at the beginning of inspiration.[46] The consequences of this type of inhalation error are dealt with in the discussion section.

Effect of DPI technique on clinical efficacy of medications

It is reasonable to hypothesise that to be effective inhaled therapies must be delivered to local sites of action within the lung in sufficient quantities. Of note, few studies have addressed the clinical impact of poor inhaler. For example, Molimard et al.[12] showed that overall treatment efficacy was compromised in about 12% of patients using the Aerolizer® or the Diskus®, compared to 32% and 28% of the patients using the Turbuhaler® and pMDIs, respectively. Interestingly, overestimation of good inhalation by general practitioners (GPs) was maximal for the Turbuhaler® (24%) and lowest for the Diskus® (9%).[12] Only 70–80% of the patients, according to the GPs, inhaled the drug dose through their DPIs correctly.[12] Patients who improved their inhalation technique showed significant reduction in the frequencies of total and nocturnal asthma symptoms, as well as β_2-agonist usage.[13]

Hesselink et al.[5] showed that about 24% of patients using DPIs made at least one critical error causing detrimental effects on effective asthma management. Although not statistically significant, chronic cough, wheezing and low total scores in health-related quality of life questionnaire were associated with incorrect inhalation technique. In addition, Pedersen et al.[6] showed that in children using the Rotahaler®, there was a statistically significant negative correlation between the numbers of errors and the increase in forced expiratory volume in 1 s (FEV_1). Coordination problems seemed to be more important than other errors in influencing lung function.[6] Others have shown that efficient DPI technique is associated with improved clinical outcomes.[7]

Discussion

In this systematic review, we have analysed studies aimed at evaluating the quality of inhalation technique with well-established DPIs in both adult and paediatric patients with asthma or COPD. We found that a large proportion of patients do not use established DPIs correctly. Furthermore,

Table 4 Most frequent errors by device made by asthma or COPD patients.

Inhaler	1st most frequent error	2nd most frequent error	3rd most frequent error
Rotahaler®	No exhalation before inhalation	No breath hold	Incorrect inhaler position
Diskhaler®	No exhalation before inhalation	Incorrect dose metering	No breath hold
Turbuhaler®	No exhalation before inhalation	Incorrect inhaler position	No breath hold
Diskus®	No exhalation before inhalation	No breath hold	Incorrect dose metering
Cyclohaler®	No exhalation before inhalation	No breath hold	Incorrect inhaler position
Aerolizer®	No exhalation before inhalation	No breath hold	Incorrect dose metering
Ingelheim inhaler®*	No exhalation before inhalation		
Autohaler®*	No exhalation before inhalation	No breath hold	Incorrect mouthpiece positioning

*Only one study.

common errors made by a significant proportion of patients were failure to exhale before inhaling through the device, incorrect positioning of the inhaler, incorrect loading and positioning of the device, failure to forcefully and deeply inhale through the device and patients' failure to hold their breathe hold after inhalation. All these errors may lead to insufficient drug delivery, which adversely influences drug efficacy and may contribute to inadequate control of asthma and COPD. A further important point emerging from this review is that the problem of incorrect use of DPIs is seriously underestimated by healthcare professionals.

One of the most important factor for the correct use of DPIs is the generation of a forceful and deep inhalation through the device.[3] However, many patients are unable to generate sufficient inspiratory airflow to use their DPIs correctly, resulting in poor drug release and low pulmonary deposition.[3] This is particularly true for elderly patients, children and those with severe airflow limitation.[3] The particle size of drug generated by DPIs is also critical for therapy success, as the size of the drug particle dictates deposition patterns within the lung.[3] With DPIs, the respirable particle fraction and consequently drug deposition are dependent on inspiratory flow rate achieved by the patient. This dependency has been clearly shown with the Turbuhaler®.[46] In fact, it has been shown that, if patients inhale maximally through the Turbuhaler® at the start of the inhalation manoeuvre, most of the emitted particles have a diameter between 1 and 6 μm and so would be deposited in the lung. If, however, the patient starts to inhale slowly at first and gradually increases the force of their inhalation effort, then the diameter sizes of the emitted particles increase substantially resulting in higher drug deposition in the mouth and oropharynx.[46] Furthermore, the clinical significance of inhalation speed seems to vary with particle size.[47] While small particles (i.e. 1.5 μm diameter) have a comparable effect on FEV_1 regardless of inhalation speed, larger particles (i.e. 3–6 μm diameter) exert a greater bronchodilator effect when inhaled at a slower speed.[47] The situation is further complicated by the fact that the ideal particle size can vary depending on the inhaled active drug. For example, inhaled β_2-agonists should be ideally separated into relatively large aerosol particles (i.e. >3–6 μm) which are mainly deposited in the large airways where they exert their greatest effect whist minimising systemic effects.[47] In contrast, it is likely that inhaled corticosteroids would exert greatest effect if delivered as smaller particles which can reach the peripheral lung regions and corresponding sites of inflammation.

In the present systematic review, every effort was made to conduct a comprehensive literature search of both primary and secondary sources. MEDLINE (1966–2005) and EMBASE (1988–2005) were thoroughly searched, and a manual search of the 15 most popular respiratory journals was conducted assessing the titles and abstracts of all articles in these journals and scanning all references from the publications identified in the search of the primary sources. Using these search strategies, 50 articles were identified which provided information on use and misuse of DPIs in the clinical setting. However, our literature search could be not exhaustive as it did not include a search of Science Direct, PubMed or Scopus databases. In addition, the search term 'dry powder inhaler' may not have been sufficient to pick up all relevant papers.

By their nature most studies examining inhalation technique are subjective by design, as they do visual assessment of patient inhaler technique measured against a pre-defined checklist of device-specific correct steps. This type of study design raises the possibility of observer bias and the likelihood of poor intra-observer repeatability. To reduce the subjective nature of assessment of patients' inhalation technique, Kamin et al.[36] used a new computer-based device to evaluate the inhalation technique of patients using the Turbuhaler®, Autohaler® or Diskus®. Interestingly, the results of that objective study mirrored the results of the subjective studies.

Inability of patients to correctly use their inhaler device may be a direct consequence of insufficient or poor inhaler technique instruction. Training apparently results in a more efficient use of established DPIs,[7,48,49] but these training sessions must be repeated, and the results checked at regular intervals. The quality of the initial instruction is of paramount importance for the outcome of inhalation therapy.[6,50] Written instruction alone is inadequate in teaching correct inhalation technique. Verbal instruction and technique assessment and reassessment are essential for patients to achieve proper technique.[21] This necessitates dedicated resources, which may be a problem in the current cost-containment environment. As many as 25% of patients have never received verbal inhaler technique instruction.[21,51] Those who have received some inhaler instruction reveal that this is almost always of less than 10 min duration,[33,52] with no follow-up assessment in 45% of cases.[33] Follow-up checks on inhaler technique are important when one considers that as early as 3 days after successful instruction, more than one-third of patients no longer use their DPI correctly.[21] Interestingly, patients who receive inhalation instructions at least once more after the initial instruction have better inhalation technique compared with those who received a single inhalation instruction at the time of prescription.[41] Training in correct inhaler use rather than instructor demonstration appears to be important.[42,43] Training devices to optimise patients' breathing whilst using a DPI have now been developed. These devices are easy to use and measure patient's inspiratory flow, so that inhalation technique can be learned quickly, even by children, and checked by a doctor or practice nurse. One such training device, the Mag-Flo® (Fyne dynamics Ltd., UK), uses a magnetic flow sensor and is attached by means of an adaptor to the inhaler or training placebo.[53] When a patient inhales properly, the magnetic flow sensor is activated, switching on a battery powered green LED that can be seen by the patient. If the patient inhales too strongly or too softly the light goes out.[53] The In-Check Dial™ (Clement Clarke International Ltd., UK) is another training device which can be used to train patients to inhale correctly through DPIs and can be used to identify the most suitable inhaler for each individual.[54] It is a hand-held inspiratory flow measurement device with a dial top which can accurately simulate the resistance of a wide variety of DPIs currently on the market.[54] Although these training devices are useful for training patients how to inhale through a device, they obviously do not teach patients how to hold, prime and position their inhaler device for optimum benefit.

The incorrect use of DPIs is not confined to patients. Healthcare professionals typically use DPIs poorly.[17] Demonstration skills and knowledge scores of medical personnel for the use of both the Turbuhaler® and Diskus® have been shown to be substantially lower than that for a pMDI.[53] Medical personnel responsible for teaching the correct use of inhalation devices are therefore lacking in basic knowledge and user skills. This probably contributes to patients' poor technique when using these devices. To ensure correct advice is provided to patients, healthcare professionals should be well versed in how to operate the various devices used by their patients and they should have access to demonstration devices. Education of healthcare professionals significantly improves their inhaler technique.[18] In addition, regular ongoing training should be provided to ensure that clinicians retain these skills.

In conclusion, although DPIs are thought to be easier to use than pMDIs, many patients with asthma or COPD still are not confident using them correctly. Regular assessment and reinforcement of correct inhalation technique by health professionals and caregivers are essential to improve disease management. The ideal inhalation device should be refillable, versatile enough to be used potentially for any inhaled medication for asthma and COPD, and immune to dampening by breathing back into the device. Furthermore, it should provide visual and auditory feedback and a dose counter which resets after a correct inhalation manoeuvre confirming not only that inhalation has occurred, but also that an inhalation is sufficient to deliver the drug. Such a device, with feedback mechanisms which guide patients through the correct inhalation manoeuvre, may improve inhalation technique and, thereby, asthma and COPD management.

Conflict of interest statement

Name	Conferences, talks	Research grants	Consultant	Educational grants
Peter Barnes	Altana/Nycomed, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Meda AB		Altana/Nycomed, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Meda AB	
Marielle Broeders			Meda AB	
Lorenzo Corbetta	Meda, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Menarini		Meda AB	Altana/Nycomed, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Meda, Chiesi
Chris Corrigan	Schering-Plough, Allergy Therapeutics, Meda AB, UCB Pharma	GlaxoSmithKline Novartis, ALK-Abello, Allergy Therapeutics	Meda AB, GlaxoSmithKline, Novartis, Merck Sharpe Dohme, Allergopharma, Joachim Ganzer AB	
Graham K. Crompton	Meda AB		Meda AB	
Richard Dekhuijzen	GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Zambon	AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim Actelion, Altana, Teva	AstraZeneca, GlaxoSmithKline, Merck, Meda AB, Altana, Boehringer Ingelheim	
Jean Christophe Dubus	GlaxoSmithKline, Ivax, AstraZeneca	Roche Aerogen Pari	Novartis Meda AB	
Federico Lavorini	Menarini Industrie Farmaceutiche, AstraZeneca, Pfizer		Meda AB	
Mark Levy	AstraZeneca, GlaxoSmithKline, Ivax, 3M, Novartis,	Ivax, Boehringer, Ingelheim, GSK,	AstraZeneca, GlaxoSmithKline, Ivax, 3M, Novartis,	

	MSD, Altana Meda AB, Trinity Chiesi, Boehringer Ingelheim, Ranbaxy, Innovata Biomedica, Schering Plough	Schering Plough, AstraZeneca	MSD, Altana Meda AB, Trinity Chiesi, Boehringer Ingelheim, Ranbaxy, Innovata Biomedica, Schering Plough
Antoine Magnan	MSD, Stallergènes, Astra-Zeneca, Novartis, Meda,. Boehringer Ingelheim	UCB, Novartis	Astra-Zeneca, Novartis, Meda AB
Joaquin Sanchis	Astra Zeneca, Meda AB	Novartis, AstraZeneca	GlaxoSmithKline, AstraZeneca, Ferrer, Meda AB
José L. Viejo	GlaxoSmithKline, AstraZeneca, Boehringer Ingelheim, Pfizer, Zambon, MerckSharpDome		GlaxoSmithKline, Zambon, Meda AB, Boehringer Ingelheim, Pfizer
Thomas Voshaar	Boehringer Ingelheim, Pfizer, Asche Chiesi, UCB, Meda AB, Altana, GlaxoSmithKline, Novartis, MSD, TEVA, 3M		Boehringer Ingelheim, Pfizer, Meda AB, MSD

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